## REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

### I. CLAIM STATUS AND AMENDMENTS

Claims 21-31 were pending in this application when last examined.

Claims 12, 13, 15-17, 21, 23, 25, 26, 28 and 29 were examined on the merits and stand rejected.

Claims 14, 18-20, 22, 24, 27, 30 and 31 were withdrawn as non-elected subject matter.

Claim 12 is amended to correct a typographical error.

Claims 16 is amended in a non-narrowing manner to use proper Markush style language. Support can be found in the disclosure, for example, at page 11, lines 29-30 and in original claim 16.

No new matter has been added by the above claim amendments.

The specification is amended to include appropriate section headings to conform to U.S. practice. Support for the newly added brief description of Figure 1 can be found in the disclosure at page 10, lines 26-30. No new matter has been added.

Applicants note that the above claim amendments are intended to address matters of form only as they are not intended to affect the scope of the claims. Accordingly, if the next Office Action on the merits includes a new rejection of one or more claims, the Action must be non-final.

Applicants are submitting the present Amendment without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be disclaimed by virtue of this response (although none is believed to be), and explicitly reserve the right to pursue some or all of such subject matter, in Divisional or Continuation Applications.

Applicants thank the Examiner for the careful examination of this case and respectfully request reexamination and reconsideration of the case, as amended. Below Applicants address the rejections in the Office Action and explain why the rejections are not applicable to the pending claims as amended.

## II. OBJECTION TO THE SPECIFICATION

The specification was objected for being in improper format for not containing appropriate section headings, in particular, a Brief Description of the Drawings, for the reasons on pages 3-5 of the Office Action.

The present amendment overcomes this concern by amending the specification, where appropriate, to include section

headings, including a Brief Description of the Drawings for Figure 1 and to conform to U.S. practice. Thus, withdrawal of the objection is solicited.

**III. CLAIM OBJECTION**

Claim 29 was objected to for the minor informality of allegedly not further limiting the claim from which it depends (i.e., claim 16) for the reasons in item 2 on page 5 of the Office Action.

The present amendment overcomes this objection by amending claim 16 in a non-narrowing manner to proper Markush style language so that the claim can contain one or more of the recited elements. Accordingly, claim 29 now appropriately further limits claim 16 to one element.

Withdrawal of the objection is requested.

**IV. PROVISIONAL DOUBLE PATENTING REJECTION**

Claims 12, 13, 15-17, 21, 23, 25, 26, 28 and 29 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being obvious over claims 10 and 11 of copending application serial No. 10/588,186 for the reasons in item 4 on page 7 of the Office Action.

Applicants respectfully traverse this rejection. Applicants submit that the instant claims are not directed to the same invention as claims 10 and 11 of the '186 application. In

this respect, the claims in the '186 application relate to a process for specifically crosslinking polymers in order to obtain a specific structure that, of course, can be grafted as in the present application, but provides a matrix having particular rheological properties not present in the matrix of the claims of the present application, which intends to protect the matrix against attacks from components of the body in which it is injected.

For these reasons, it is believed that claims 12, 13, 15-17, 21, 23, 25, 26, 28 and 29 are not obvious over claims 10 and 11 of the '186 application. Thus, the rejection should be withdrawn.

In the event that the Office disagrees and maintains the rejection, then Applicants will consider the possibility of submitting a Terminal Disclaimer.

## V. WRITTEN DESCRIPTION REJECTION

Claims 12, 13, 15-17, 21, 23, 25, 26, 28 and 29 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in item 6 on pages 8-9 of the Office Action.

This rejection is respectfully traversed.

The Office is concerned with the phrase "non-polymeric chains having antioxidant properties or properties for inhibiting reactions of degradation of said matrix" in independent claim 12.

On page 8 of the Action, the Office notes that the specification, at page 8, lines 21-23, defines non-polymeric chains as vitamins, enzymes and cyclic molecules and argues that:

> Vitamins, enzymes and cyclic molecules are large genera that encompass highly variant members with a myriad of possibilities. The specification provides insufficient written description as to what types of activity is necessary to inhibit degradation of the polymer matrix. For example, do all cyclic molecules prevent matrix degradation or are certain size rings and/or chemical compositions (e.g., certain heterocyclic rings) required in order to degradation to be inhibited?

Applicants disagree with the Office's position.

The test for sufficiency of written description is whether the disclosure reasonably conveys to the artisan that the inventor had possession at the time of filing of the subject matter which is claimed. M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2163, I, 2100-159, 1st column, 2nd paragraph.

This test may be satisfied by: (1) a reduction to practice; (2) a reduction to drawings/chemical formulas; (3) a disclosure of relevant identifying characteristics, such as structure or other physical and/or chemical properties, to sufficiently describe the claimed invention in full, clear, concise and exact terms; (4) a disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure; (5) a sufficient description of a representative number of species; or (6) a combination of

the above, sufficient to show the inventors were in possession of the invention. M.P.E.P. (Eighth Ed., Rev. 6 (September 2007) at § 2163,II, A, 3a(i)-(ii).

Applicants respectfully submit that one skilled in the art knows that the phrase "non-polymeric chains having antioxidant properties or properties for inhibiting reactions of degradation of said matrix" encompasses a very large number of species.

However, in reply to the Office's inquiry as to what types of activity is necessary to inhibit degradation of the polymer matrix, it is respectfully submitted that any type of activity is useful to inhibit the degradation of the polymer matrix. For instance, all cyclic molecules contained in a grafted chain have an activity of preventing matrix degradation in that the grafted chain has a free movement of the non-grafted end that may physically mask the sensible sites of the matrix from the attacks of the degrading agents.

The grafted chains present with a grafting rate of 10-40% have an effect of steric hindrance due to this rate and the movement of the non-grafted end of the chains. This steric hindrance is obtained independently of the anti-oxidant or other inhibiting properties. See, for instance, the disclosure at page 10, lines 13-20.

Applicants believe that such disclosure constitutes: (1) a disclosure of relevant identifying characteristics, such as

structure or other physical and/or chemical properties, to sufficiently describe the claimed invention in full, clear, concise and exact terms; and (2) a disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure, sufficient to show the inventors were in possession of the invention.

In addition, on pages 9-10, the specification describes in detail the use of vitamin C, vitamin A, Melatonin, etc. Such is even exemplified in the examples. It is respectfully submitted that this disclosure amounts to a reduction to practice sufficient to show the inventors were in possession of the invention.

Therefore, Applicants respectfully submit that the specification provides full written description support for the non-polymeric chains of claim 12. For this reason, the above written description rejection is believed to be untenable and should be withdrawn.

**VI. INDEFINITENESS REJECTIONS**

Claims 12, 13, 15-17, 21, 23, 25, 26, 28 and 29 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons in item 8 on page 9 of the Office Action. Specifically, the Office argues that the term non-polymeric chains" encompasses enzymes that can be protein-based and RNA based and as such the term encompasses one genera

belonging to this category is polymeric in nature. This rejection is respectfully traversed.

Applicants recognize that enzymes are polymers of several amino-acids or of nucleotides polymers (ribozymes), but differ from the polymers of the matrix in that they are polymers of specific and different monomers (amino-acids of natural origin), whereas the polymers of the matrix are homopolymers or copolymers of repetitive units of few monomers. For this reason, it is believed that the skilled artisan would readily understand the metes and bounds of the noted claim language. The claims are thus clear and definite.

This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Claims 15 and 21 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons in item 9 on pages 9-10 of the Office Action. This rejection is respectfully traversed.

The "number of moles of the cross linking agent ensuring the linking of the polymer chains" is expressed as the theoretical cross linking rate as the real cross linking rate is difficult to determine in actual practice. But the reactions conditions are such that they ensure a maximal cross linking rate which tends to approach the theoretical one.

For this reason, it is believed that the skilled artisan would readily understand the metes and bounds of the

noted claim language. Thus, the rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Claims 16, 17, 23, 25, 26, 28 and 29 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons in item 10 on pages 10-11 of the Office Action. This rejection is respectfully traversed.

It is acknowledged that claims 16, 17, 23, 25, 26, 28 and 29 recite additional components that might be contained in the matrix. However, it does not matter whether they are not overlapping in their definition. It is clear that these additional components are not grafted and are thus all dispersed,

- either because they have been introduced in the matrix during the grafting phase but still remain ungrafted because of the progressive unavailibity of the grafting sites (already grafted or made "invisible" by the grafted chains); or

- because they have been introduced in the matrix after grafting and remain ungrafted.

Both antioxidant chains and other chains inhibiting degradation may (not must) be grafted and ungrafted. However as explained below, a specific rate of grafting must be obtained, the ungrafted amount of other components is free.

For this reason, it is believed that the skilled artisan would readily understand the metes and bounds of the noted claim language. Thus, the rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

**VII. OBVIOUSNESS REJECTIONS**

Claims 12, 13 and 17 were rejected under 35 U.S.C. § 103(a) as obvious over NGUYEN (EP 0749982A) for the reasons in item 14 on pages 12-13 of the Office Action.

Claims 12, 13, 16, 23, 26 and 29 were rejected under 35 U.S.C. § 103(a) as obvious over NGUYEN in view of RAMAMURTHI (J. Biomed. Mater. Res., 2002) for the reasons in item 15 on pages 13-14 of the Office Action.

Claims 12, 13, 15 and 21 were rejected under 35 U.S.C. § 103(a) as obvious over NGUYEN in view of BOLOTIN (PGPub 2003/0224974) for the reasons in item 16 on pages 14-15 of the Office Action.

Claims 12, 15, 25 and 28 were rejected under 35 U.S.C. § 103(a) as obvious over NGUYEN in view of BOLOTIN and RAMAMURTHI for the reasons in item 17 on pages 15-16 of the Office Action.

These rejections are respectfully traversed as applied to the amended claims.

It is well established that to support a *prima facie* case of obviousness, the Office must provide a rationale showing that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions to yield predictable results. *See, KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 U.S.P.Q.2d 1385, 1395

(2007); and M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2143.02.

As amended, independent claim 12 recites

> 12. A complex matrix comprising: at least one biocompatible polymer of natural origin, cross linked with a cross linking agent of a bi- or polyfunctional molecule selected from the group consisting of epoxides, epihalohydrines and divinylsulfone and wherein said polymer has grafted chains having a molecular weight less than 50,000 Da, selected from polymers of natural origin of small size, and/or non-polymeric chains having antioxidant properties or properties for inhibiting reactions of degradation of said matrix, and
>
> wherein the quantity of grafting is defined as being the ratio between the number of moles of grafted molecules and the number of moles of units of the polymer, from 10 to 40%.

Applicants respectfully submit that the combined prior art references fail to disclose or suggest each and every element of the claimed matrix. In this regard, it is believed that NGUYEN does not describe the same grafted polymers. Of course, NGUYEN discloses a cross-linked polysaccharide grafted with antioxidant in order to limit the degradation due to hydroxy radicals.

However, in NGUYEN, the rate of grafting is limited to 1 equivalent of antioxidant per 10 equivalents of polysaccharide units, and preferably to 1 equivalent for 400 units. These are values are much lower than the grafting rate of 10-40% of independent claim 12 of the present application. As such, NGUYEN

cannot be said to disclose or suggest the rate of grafting of 10-40% in claim 12.

Further, while one skilled in the art might eventually assume that an increase in the grafting rate will increase the resistance to degradation, the teaching of the NGUYEN clearly did not suggest such, especially in view of the preferred values in NGUYEN that are significantly lower than the maximum value by itself which is lower than in claim 12 of the present application.

Accordingly, of ordinary skill in the art, upon reading NGUYEN would still wonder about the consequences of this high grafting on the visco-elastic properties of the final product as he would know that an increase in the crosslinking rate increases the viscosity of the final product which thus decreases its injectability. Grafting of chains, even if they have a molecular weight less than 50,000 Da could be considered as an increase in the properties of cross-linking and expected to result in an increase of the viscosity of the cross-linked and grafted polymer matrix beyond that of the limit due to its injectability. This is surprisingly not the case in the present invention. Thus, for these reasons, it is believed that: (1) the matrix of claim 12 achieves surprising and unexpected results over NGUYEN; and (2) the reference teachings are not predictive of the claimed invention, in other words, there is no reasonable expectation of

successfully modifying the teachings in NGUYEN to arrive at claim 12.

Furthermore, NGUYEN only considers the use of antioxidants at a lower grafting rate. NGUYEN did not teach or suggest an action of the grafted chains due to steric hindrance.

For these reasons, it is respectfully submitted that NGUYEN fails to render obvious independent claim 12. Thus, claim 12 and all claims dependent thereon are novel and patentable over NGUYEN. Thus, the 103(a) obviousness rejection over NGUYEN is believed to be overcome.

As to the remaining 103(a) obviousness rejections over NGUYEN in view of RAMAMURTHI and/or BOLOTIN, Applicants respectfully submit that the secondary references of RAMAMURTHI and/or BOLOTIN fail to remedy the above-discussed deficiencies in NGUYEN.

RAMAMURTHI is relied upon for disclosing divinylsulfone cross-linked HLA-based polymers. However, this is not relevant, as in the present invention of claim 12, it is the grafting rate which constitutes the novel and inventive step as discussed above. The same can be said for the other secondary reference of BOLOTIN. The combined teachings of these references relate to the rate of cross-linking, which is not the important aspect of the invention of claim 12. Instead, it is the rate of grafting of cross-linked polymers in the matrix (i.e., grafting rate of 10-40% of independent claim 12).

For these reasons, it is clear that RAMAMURTHI and BOLOTIN fail to disclose or suggest this novel and inventive feature (i.e., the grafting rate of 10-40%) of independent claim 12. Thus, claim 12 and all claims dependent thereon are novel and non-obvious over NGUYEN alone, or taken with RAMAMURTHI and/or BOLOTIN.

For these reasons, the above-noted 103(a) obviousness rejections of NGUYEN alone, or taken with RAMAMURTHI and/or BOLOTIN are untenable and should be withdrawn.

**VIII. CONCLUSION**

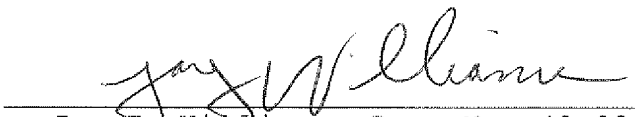
In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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